Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Thyroid Function Abnormalities in Patients with Different Stages of Chronic Kidney Disease

Mohammad Momin Uddin Chowdhury[1*], Saima Hoque[2], Shalina A.Shahin[3], Mohammed Aminul Hoque Sarker[4], Sandwip Talukdar[5]

[1]RMO (Medicine), 250 Bed District Hospital, Habiganj, Bangladesh
[2]Private Practitioner, Life care Hospital Ltd, Dhaka, Bangladesh
[3]Medical Assistant, Tulane University School Of Public Health And Topical Medicine, 1440 Canal Street, New Orleans, LA USA
[4]Superintendent (Medicine), 250 Bed District Hospital, Habiganj, Bangladesh
[5]Assistant Professor, Dept. Of Forensic Medicine, North Bengal Medical College, Sirajganj, Bangladesh

DOI: 10.36347/sjams.2022.v10i09.020 | **Received:** 09.08.2022 | **Accepted:** 15.09.2022 | **Published:** 20.09.2022

***Corresponding author:** Mohammad Momin Uddin Chowdhury
RMO (Medicine), 250 Bed District Hospital, Habiganj, Bangladesh

Abstract **Original Research Article**

***Introduction*:** Thyroid hormones are crucial for renal development and physiology. Thyroidal hormones affect the cardiovascular system through their influence on renal blood flow as it modulates the glomerular function, the tubular secretory and absorptive capacities as well as the electrolyte pumps and the kidney structure. ***Objective*:** To assess the thyroid function abnormalities in patients with different stages of chronic kidney disease. ***Materials and Methods*:** The cross sectional observation study was conducted in Department of Medicine, 250 Bed District Hospital, Habiganj, Bangladesh from January to April 2021. Included 54 CKD patients not on dialysis, who are only on conservative management. ***Results*:** In our study the age matched graph shows that maximum number of patients in the category of 40-49 years with 8 males and 6 females, 50- 59 years had 8 males and 6 females, whereas between 60 to 69 years there were 6 males and 6 females. The extreme age groups had few patients chronic kidney disease above 70 there were 2 females and 2 males between 18-29 years there were 3 males and 3 females and 30-39 years had 1 male and 3 females. In our study the number of chronic kidney patients having low T3 were 39 which constitutes 72.2%,the patients with normal T3 were 12 constituting 22.2% and those with high T3 were 3, suggesting primary hyperthyroidism, so excluding them 75% of our patients had low T3 syndrome. In our study 39 patients had low T3, 26 had low T4 with 49 patients being normal TSH, only 4 had high high TSH. Excluding patients with primary hypothyroidism. Patients with low T3 low T4 were clustered in more towards end stage renal disease with 60%. Patients also were in moderate number with low T3 and low T4 in stage 4 chronic kidney disease. 20% in stage 3 chronic kidney disease T4 and TSH were almost normal with only 10% patients had low T3 syndrome. In stage 2 chronic kidney disease 10% had low T3, low T4 with rest being normal TSH. In our study patients with low T3 were 37 accounts for nearly 69% and T3 were 14 (26%). Only 3 patients had primary hypothyroidism-5.5%. In our study low T3 syndrome had ranged from 0.67-1.89 of the mean with a standard deviation of 0.52-0.86. ***Conclusion*:** In our study we aim to see the prevalence of low T3 syndrome in different stages of CKD which is a state of physiological benefit in preserving the proteins lost through the Kidneys in CKD patients and since CKD is progressed in hyperthyroidism state it is a protective mechanism in restoring the CKD status. A Thorough knowledge of these is required for optimum treatment of thyroid in CKD patients.

Keywords: Glomerular Filtration Rate, Chronic Kidney Disease, Thyroid Stimulating Hormone.

INTRODUCTION

Thyroid hormones are crucial for renal development and physiology [1]. Thyroidal hormones affect the cardiovascular system through their influence on renal blood flow as it modulates the glomerular function, the tubular secretory and absorptive capacities as well as the electrolyte pumps and the kidney structure [2, 3]. Chronic kidney disease is increasing in prevalence worldwide with irreversible loss of nephrons and metabolic, endocrine, secretory and excretory functions. It affects every system in body including the thyroid hormone [4].The reduced elimination of iodine in CKD, increases iodide levels thereby blocking thyroid hormone production (wolff chaikoff effect) [5]. Chronic Kidney Disease is associated with low levels of serum total and free T3, T4 and reverse T3 [6]. Thyroid Stimulating Hormone is usually normal and found to be

in euthyroid state [7]. Many studies have reported hypothyroid, hyperthyroid and euthyroid states in Chronic Kidney Disease. Extreme variation in the thyroid function results in changes in different clinical renal parameters such as glomerular filtration rate (GFR), urine specific gravity, urinary protein/ creatinine ratio and markers of tubular function. Reciprocally, kidney disease status can influence circulating thyroid hormones [8] as the kidney is responsible for the metabolism and excretion of thyroid hormones. For instance, due to reduced deiodinase activity, tissue and circulating levels of the active form of the thyroid hormone, T3, are low in kidney disease [79]. Also, as a result of reduced renal excretion, inorganic iodide generated by residual deiodinase activity accumulates in CKD stages 4 and 5, which in turn dampens thyroid hormone synthesis. The relationship between severity of renal failure and thyroid dysfunction is unclear [10,11]. This abnormality is not associated with increased conversion of T4 to the metabolically inactive reverse T3 (rT3), since plasma rT3 levels are typically normal. This finding differentiates the uremic patient from patients with chronic illness in which the conversion of T4 to T3 is similarly reduced, but the generation of rT3 from T4 is enhanced. In addition to decreased production, low levels of total T3 also may reflect reduced protein binding [12]. The kidney normally contributes to the clearance of iodide from the body. With advancing renal failure iodide excretion is diminished leading sequentially to an elevated plasma inorganic iodide concentration and an initial increment in thyroidal iodide uptake. Thyroid gland and chronic kidney disease: Abnormalities in the structure and function of thyroid gland and the metabolism and plasma conc. of thyroid hormones are common in patients with CKD. Various thyroid disorders-hypothyroidism, goiter, thyroid modules & thyroid carcinoma are seen in patients with CKD [13]. Based on research studies Low T3 is the most common laboratory finding6 & subclinical hypothyroidism is most common thyroid disorder found in CKD patients [14]. TSH levels are usually normal with and altered circadian rhythm. This study is based on mainly seeing the importance of interactions between the thyroid gland functions and renal function is chronic kidney disease patients and to co-relate the levels of thyroid hormones with eGFR.

MATERIALS AND METHODS

The cross sectional observation study was conducted in Department of Medicine, 250 Bed District Hospital, Habiganj, Bangladesh from January to April 2021. Included 54 CKD patients not on dialysis, who are only on conservative management.

Inclusion Criteria:

- Age more than 18 years.
- Patients with Chronic Kidney Disease on conservative management.
- Patients with Chronic Kidney Disease who are willing to participate in the study and give informed written consent.

Exclusion Criteria:

- Patients on Dialysis.
- Acute illness, diabetes mellitus, liver disease, recent surgery, trauma.
- Nephrotic range proteinuria or hypoalbuminemia.
- Patients who have received drugs altering thyroid profile like Amiodarone, Phenytoin, Beta blocker, Steroids, Estrogen, iodine compounds.

Statistical Analysis

Simple random sampling. T test was used for continuous variables and chi square test for categorical variables. ANOVA test was used to compare three groups. A p value of <0.05 was considered statistically significant.

RESULTS

Table 1: Analysis of Age and Gender Distribution OF CKD (N=54)

Age	Male	Female
18-29yer	3	3
30-39yer	1	3
40-49yer	8	6
50-59yer	8	6
60-69yer	6	6
70-79yer	1	1
80-90yer	1	1
Total	28	26

In our study the age matched graph shows that maximum number of patients in the category of 40-49 years with 8 males and 6 females, 50- 59 years had 8 males and 6 females, whereas between 60 to 69 years there were 6 males and 6 females. The extreme age groups had few patients chronic kidney disease above 70 there were 2 females and 2 males between 18-29 years there were 3 males and 3 females and 30-39 years had 1 male and 3 females. There is a cluster of cases in middle age and with equal sex distribution.

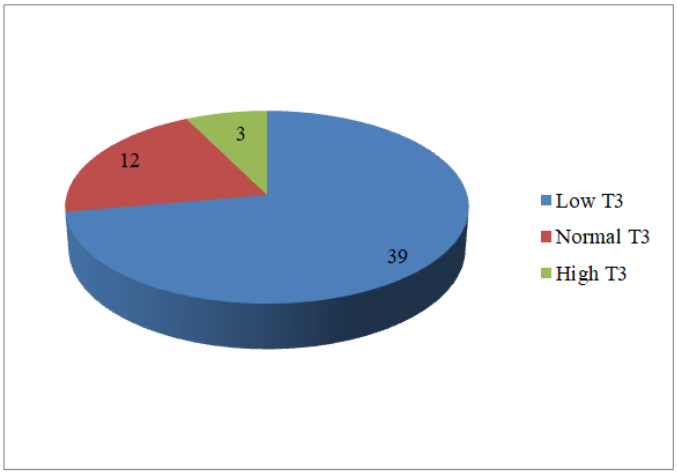

Fig-1: Pie Diagram Showing.

In our study the number of chronic kidney patients having low T3 were 39 which constitutes 72.2%, the patients with normal T3 were 12 constituting 22.2% and those with high T3 were 3, suggesting primary hyperthyroidism, so excluding them 75% of our patients had low T3 syndrome.

Table 2: Analysis of T3, T4, TSH (N=54)

Thyroid status	No of patients with normal value	Low value	High value
T3	**11**	**39**	**4**
T4	**28**	**26**	**Nil**
TSH	**49**	**Nil**	**5**

In our study 39 patients had low T3, 26 had low T4 with 49 patients being normal TSH, only 4 had high high TSH. excluding patients with primary hypothyroidism.

Table 3: Bar Diagram (N=54)

	Low T3	Low T4	High TSH
GFR<15	30	7	2
GFR 15-30	4	3	2
GFR 30-60	2	0	0
GFR>60	1	1	0

Patients with low T3 low T4 were clustered in more towards end stage renal disease with 60%. Patients also were in moderate number with low T3 and low T4 in stage 4 chronic kidney disease. 20% in stage 3 chronic kidney disease T4 and TSH were almost normal with only 10% patients had low T3 syndrome. In stage 2 chronic kidney disease 10% had low T3, low T4 with rest being normal TSH. In our study patients with low T3 were 37 accounts for nearly 69% and T3 were 14 (26%). Only 3 patients had primary hypothyroidism-5.5%.

Table 4: Incidence of low T3 syndrome in CKD (N=54)

Primary Hypothyroidism	Low T3	Normal
Yes	**3**	**0**
No	**37**	**14**

Table 5: Statistical Analysis (N=54)

Creatinine Clearence (ml/m)	T3		T4		TSH	
	Mean	SD	Mean	SD	Mean	SD
<15	0.67	0.52	5.78	2.30	4.47	5.50
15-30	0.72	0.47	6.04	2.28	4.60	7.97
30-60	1.05	0.73	7.55	2.63	5.35	8.10
>60	1.89	0.86	8.22	2.72	5.96	9.01

In our study low T3 syndrome had ranged from 0.67-1.89 of the mean with a standard deviation of 0.52-0.86.

DISCUSSION

The present study was aimed to assess the prevalence of thyroid dysfunction in chronic kidney disease patients and to determine the correlation between thyroid dysfunction and severity of renal disease. Various studies were conducted about thyroid dysfunction and severity of chronic kidney disease and have shown different results. Since thyroid profile undergoes changes due to dialysis [15]. In our study, chronic kidney disease patients only on conservative management were studied. Dialysis also changes the previous serum thyroid hormone status in patients with renal failure several studies have observed a link between CKD and hypothyroidism [16, 17]. But there are not many studies correlating low T3 with severity or stage of CKD. In our study none of the patients had clinical or biochemical features Hyperthyroidism. In our study 54 patients of CKD who were on conservative management fulfilling the criteria for Chronic kidney disease, the maximum number of patients in the category of 40-49 years with 8 males and 6 females, 50-59 years had 8 males and 6 females, whereas between 60 to 69 years there were 6 males and 6 females. The extreme age groups had few patients chronic kidney disease above 70 there were 2 females and 2 males between 18-29 years there were 3 males and 3 females and 30-39 years had 1 male and 3 females. There is a cluster of cases in middle age and with equal sex distribution. In our study the duration of symptoms of CKD varied from 4 months to 8 months, mean duration being 6.07 months and the creatinine clearance varied from 4 ml/minute-60 ml/minute. In our study the number of chronic kidney patients having low T3 were 39 which constitutes 72.2%, the patients with normal T3 were 12 constituting 22.2% and those with high T3 were 3, suggesting primary hyperthyroidism, so excluding them 75% of our patients had low T3 syndrome. Karunanidhi A *et al*., found that thyroid hypofunction is a direct result of renal failure and serum levels of thyroxine and triiodothyronine fall progressively as renal function worsens, suggesting the severity and duration of the uremic state is a major influence on hormone synthesis [16]. Ultrasound abdomen was done in all patients, that showed features of contracted kidney in 40 patients accounting for 80% and the remaining 10 patients had loss of corticomedullary differentiation, accounting for 20%. Patients with low T3 low T4 were clustered in more towards end stage renal disease with 60%. Mohamedali M *et al*., found that the prevalence of subclinical hypothyroidism increases consistently in patients who have a decline in GFR [5]. Patients also were in moderate number with low T3 and low T4 in stage 4 chronic kidney disease. 20% in stage 3 chronic kidney disease T4 and TSH were almost normal with only 10% patients had low T3 syndrome. In stage 2 chronic kidney disease 10% had low T3, low T4 with rest being normal TSH. In our study patients with low T3 were 37 accounts for nearly 69% and T3 were 14 (26%). Only 3 patients had primary hypothyroidism-5.5%. Michael Chonchol *et al*., found that subclinical primary hypothyroidism is a relatively common condition (18%) among persons with CKD not requiring chronic dialysis, and is independently associated with progressively lower estimated GFR [14]. Out of 54 patients in our study, 48 patients had anaemia, 44 patients had normocytic normochromic anaemia in peripheral blood picture and the remaining 4 patients had microcytic hypochromic anaemia. The only Indian study directly correlating severity of CKD and Low T3 syndrome is by swaminathan K *et al*., who compared the estimated Glomerular filtration rate values with , T3,T4,TSH found a significant correlation with 66% patients having thyroid dysfunction with >50% having low T3, more severe the stage of chronic kidney disease [18, 19].

CONCLUSION

In our study of 54 CKD patients, 60% had low T3 values. Excluding hypothyroidism the T3 level was low in 50% patients and T4 level was low in 20% patients. The change in serum T3 and T4 can be taken as protective to conserve protein. As the stage of CKD increases the patients with low T3 T4 level increases. The incidence of low T3 increases with age. There is a direct linear relationship with GFR and low T3 in our patients.

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